IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

In re: TESTOSTERONE	)	
REPLACEMENT THERAPY	)	Case No. 1:14-cv-01748
PRODUCTS LIABILITY LITIGATION	)	MDL No. 2545
	)	
This Document Relates To:	)	
Konrad v. AbbVie Inc. No. 1:15-cv-00966	)	
Mitchell v. AbbVie Inc. No. 1:14-cv-09178	)	

DEFENDANTS' PROPOSED PRELIMINARY JURY INSTRUCITON REGARDING THE ROLE OF THE FDA

Defendants AbbVie Inc. and Abbott Laboratories (collectively "AbbVie") respectfully submit this supplemental proposed preliminary jury instruction on the role of the FDA.

AbbVie Proposed Preliminary Jury Instruction No. 2:

Role of Federal Food and Drug Administration (FDA)

AndroGel is a prescription drug regulated by the Food and Drug Administration (or "FDA" for short). The FDA is the federal regulatory agency charged with protecting the public health by ensuring that pharmaceutical products, such as AndroGel, are safe and effective for their intended uses. To that end, and with very limited exceptions, a prescription drug may not be sold in the United States until after the FDA approves it as "safe" and "effective." The FDA has approved Testosterone Replacement Therapies (or "TRTs" for short) as safe since the 1940s, and as effective since Congress first required the FDA to evaluate effectiveness in 1962. The FDA approved AndroGel, a TRT, in 2000.

To obtain clinical evidence to support an application for authorization to sell a new drug, the manufacturer first must submit an application seeking approval from the FDA to perform scientific studies known as clinical trials. This application is known as an Investigational New Drug Application or "IND" for short. A team of scientists at the FDA reviews the data submitted

with the IND, which must establish that the new drug is safe enough for testing in humans. When the safety of the product for use in humans is in question, the FDA can and does place a hold on the initiation or continuation of clinical trials. If the FDA allows the IND to proceed, the manufacturer must then conduct a multiphase clinical trial program to study the safety and effectiveness of the drug. The FDA's regulations provide specific guidance to manufacturers regarding the design of clinical trials submitted in support of a new drug application. FDA scientists are actively involved in the design, development, and review of the clinical trials necessary to support a drug approval. The FDA also has the discretion to require manufacturers to conduct additional studies to obtain marketing approval. During this process, the manufacturer cannot conduct a study unless the FDA allows the study to proceed.

Following the clinical trials, the manufacturer submits a New Drug Application or "NDA" for short. Under the Federal Food, Drug, & Cosmetic Act, the NDA must include, among other things, "full reports of investigations which have been made" to establish that the drug is "safe and effective for use."[1] A team of scientists and regulatory experts at the FDA reviews the NDA and the submitted clinical trial data to determine whether it establishes the drug's safety and effectiveness. By this point, the FDA team is already familiar with the drug from the FDA's involvement in the clinical trial process. The FDA, alone, makes the final determination whether to approve an NDA and allow a drug to be sold in the United States. In making this determination, the FDA will approve a drug only if "substantial evidence" shows it is safe and effective if used as directed.[2]

As part of the NDA, the manufacturer also must submit proposed labeling, which must include information for prescribing physicians about the safe and effective use of the drug. For

[1] 21 U.S.C. § 355(b)(1)(A).
[2] 21 U.S.C. §355 (d)

TRTs such as AndroGel, the proposed labeling must closely track the Class Labeling Guidelines first published by the FDA in 1981. Class labeling is uniform labeling language and placement required by the FDA to address usage and safety issues believed to be relevant to all members of a single therapeutic or chemical class of products, such as TRTs. The safety issues are covered in the "Warnings and Precautions" section, among other areas of the labeling. Among other things, this section must describe clinically significant adverse reactions and other potential safety hazards. The FDA defines a clinically significant adverse reaction as an "undesirable effect" "for which there is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event."[3] In addition to the guidance provided by any applicable Class Labeling Guidelines, the FDA typically engages in extensive discussions with the manufacturer regarding the placement and language contained in the labeling. Ultimately, the FDA must approve the content and language of the initial labeling before the drug is approved for sale in the United States.

The FDA continues to regulate the manufacture and sale of a drug even after approval. For example, FDA has authority over advertising and promotion of prescription drug products. FDA asserts this authority by requiring a manufacturer to submit for FDA review the "advertising designed for promotion of the drug" "at the time of initial publication of the advertisement for a prescription drug product."[4] The FDA has an organizational unit specifically devoted to reviewing advertising and promotion for prescription drug products, the mission of which is to protect the public health by assuring prescription drug information is truthful, balanced, and accurately communicated. If that unit determines that an advertisement is not in compliance with FDA regulations, it has several options, including written correspondence in the form of Warning

[3] 21 CFR § 201.57(c)(7).
[4] 21 CFR § 314.81(b).

Letters, which are then made publicly available on the FDA's website.

In addition to monitoring prescription drug advertising, the FDA shares with the manufacturer the responsibility to monitor and evaluate new information that could impact the safety risks associated with the drug. A manufacturer is required to disclose to the FDA any adverse reactions reported during the drug's use. The FDA also independently reviews new clinical data and adverse reaction reports available from the manufacturer and from other sources, such as other manufacturers, researchers, doctors, and patients. The FDA has the authority to require amendments to the drug's labeling on the basis of its own assessment of new safety information.

At the same time, the manufacturer bears responsibility for the content of the drug's labeling at all times. The manufacturer is charged with ensuring that its warnings remain adequate for as long as the drug is on the market. In most instances, a drug manufacturer must obtain FDA approval before changing a drug's labeling. In certain cases, however, the manufacturer can unilaterally add or strengthen a warning, precaution, contraindication, or adverse reaction for its products without prior FDA approval. In that regard, a manufacturer is allowed to revise its labeling to include a warning once there is reasonable evidence of a causal association of a serious hazard with its drug; a causal relationship need not have been definitely established before a manufacturer changes its warnings. Changes to a product's warnings by a drug manufacturer without prior FDA approval may only be made on the basis of "newly acquired information."[5] This includes information from new studies or reports of adverse events, or new analysis of previously submitted data, if the studies, events, or analysis reveals risks of a different type or greater severity or frequency than previously included in submissions to the FDA. The FDA

[5] 21 CFR § 314.70(c)(6)(iii).

retains the authority to reject labeling changes made by the manufacturer, and should the manufacturer not comply with the FDA's decision, the FDA may exercise its authority to bring an enforcement action against the manufacturer. Penalties may include monetary fines, injunctions, and seizure of the drug. To avoid the need to reverse a labeling change if the FDA ultimately rejects it, manufacturers might choose to seek FDA approval prior to making any labeling changes. Source: 21 U.S.C. § 355; 21 CFR § 201.80; 21 CFR §314.70; 21 CFR §314.80; Wyeth v. Levine, 555 U.S. 555 (2009), Utts v. Bristol-Myers Squibb Co., No. 1:16-cv-05668-DLC, 2017 WL 1906875 (S.D.N.Y. May 8, 2017).

Dated: June 1, 2017

Respectfully submitted,

s/David M. Bernick

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CERTIFICATE OF SERVICE

I hereby certify that on June 1, 2017, the foregoing document was filed via the Court's CM/ECF system, which will automatically serve and send email notification of such filing to all registered attorneys of record.

/s/ Michelle Yeary